85. (Amended) The process of claim 83 wherein the step of testing the ability of the candidate substance to bind to the opioid receptor involves determining the ability of the candidate substance to activate the receptor.

F3

86. (Amended) A process for screening a candidate substance for its ability to bind to a mu opioid receptor comprising:

(a) providing a recombinant opioid receptor polypeptide encoded by a nucleic acid sequence comprising at least 35 contiguous nucleotides of SEQ ID NO:7, including the guanine nucleotide at position 389 of SEQ ID NO:7;

(b) contacting the candidate substance with the recombinant opioid receptor polypeptide; and

(c) detecting the ability of the candidate substance to bind to the recombinant opioid receptor polypeptide.

91. (Amended) The process of claim 86, wherein the nucleic acid sequence comprises the nucleotide sequence of SEQ ID NO:7.

F4

92. (Amended) The process of claim 86, wherein detecting the ability of the candidate substance to bind to the recombinant opioid receptor polypeptide involves measuring (i) the ability of the recombinant opioid receptor polypeptide to bind the candidate substance; (ii) the ability of the candidate substance to activate ion channels in a cell membrane; or (iii) modulation of ion channels in the cell membrane of part (ii).

These amendments are illustrated in Appendix A attached hereto.

II. RESPONSE TO OFFICE ACTION

A. Status of the Claims

Claims 83-101 were pending prior to the Office Action dated May 30, 2002. Claims 83, 86, 92, and 94 have been amended, as shown in appendix A. Support for the amendments may be found throughout the specification, including the originally filed claims. No new matter has been added. For the Examiner's convenience, the pending claims are attached hereto as Appendix B.

B. Various claim objections

The Action objects to claims 83, 86, 91, 92, 94 and 100 for various reasons. Some of the objection have been address by claim amendment as described herein.

1. Objection to claim 83 for containing language that was not necessary.

Applicants have amended the claims accordingly and request the removal of the objection.

2. Objection to claims 86 and 94 based on syntax.

Claims 86 and 94 read as Applicants intend them to read. The amendment proposed by the Action would alter the claims. The requirement of 35 U.S.C. §112, second paragraph, is that a person of skill in the art can ascertain the scope of the claim with reasonable certainty. The Examiner has provided no reason to object otherwise. These claims fulfill that requirement. Withdrawal of the objection is requested.

3. Objection to claim 92 based on syntax.

Applicants have amended the claims accordingly and request the removal of the objection.

C. Claims 86-90, 92-99 and 101 are supported by the specification

Claims 86-90, 92-99 and 101 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. Applicants respectfully traverse.

The Action states that the Applicants have provided no written description as to what amino acids are necessary in order to retain the mu opioid receptor characteristics. Furthermore, the Action concludes that one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus.

In order to satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. *See, e.g., Vas-Cath, Inc. v. Mahurkar*, 935 F.2d at 1563, 19 USPQ2d at 1116 and MPEP 2163(I). The Action dated 5/30/2002 does not apply the proper standard for written description. Applicants note that the claimed invention is drawn to a process of screening a candidate substance for its ability to bind a mu opioid receptor. Thus, the amino acids necessary to convey a mu opioid receptor function should not be and is not at issue as it relates to written description.

In providing written description, one must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. One skilled in the art would reasonably conclude that the inventor had possession of a recombinant opioid receptor polypeptide encoded for by a nucleic acid sequence comprising at least 35 contiguous nucleotides of SEQ ID NO:7, including the guanine nucleotide at position 389 of SEQ ID NO:7 based on the description provided for in the specification at

least on page 36 lines 10 to 18; pages 36 to 44; pages 150-153 and by SEQ ID NO:7 and SEQ ID NO:8. The ligand binding characteristics of the polypeptide are irrelevant. The claimed process is for screening a substance for its ability to bind a recombinant mu opioid receptor polypeptide. Thus, for example, the process may identify an antibody that binds a recombinant opioid receptor polypeptide encoded for by a nucleic acid sequence of 35 contiguous nucleotides of SEQ ID NO:7, including the guanine nucleotide at position 389 of SEQ ID NO:7. Furthermore, variants of a recombinant mu opioid receptor polypeptide, particularly chimeras, are described in detail at least on page 38 lines 1-9 and pages 36–44.

In addition, the Action reasons that a peptide fragment of 12 amino acids is within the scope of the claimed methods, but the specification provides no written description as to what amino acid residues are necessary for ligands to bind to these opioid receptors, or as to what other residues are necessary to produce functional opioid receptors. Applicants submit that there is nothing in the claim that limits the candidate substance to a ligand and the functionality of the polypeptide is irrelevant. Claim 86, for example, reads in part "A process of screening a candidate substance for its ability to **bind** a mu opioid receptor...detecting the ability of the candidate substance to **bind** to the recombinant opioid receptor polypeptide"(emphasis added). As described above, a recombinant opioid receptor polypeptide that encompasses the sequence distinguishing the mu opioid receptor polypeptide, namely a "polypeptide encoded by a nucleic acid sequence comprising at least 35 nucleotides of SEQ ID NO:7, including the guanine at 389 of SEQ ID NO:7," provides adequate description of polypeptides used in the claimed methods to provide one of skill in the art a reasonable certainty that the inventor had possession of the claimed invention.

In summary, the claims are directed to methods of screening a candidate substance's ability to bind to a recombinant polypeptide, which is defined as including a polypeptide encoded by a nucleic acid sequence comprising at least 35 nucleotides of SEQ ID NO:7, including the guanine at 389 of SEQ ID NO:7 (a distinguishing characteristic of the mu opioid receptor), and not to mu opioid receptors *per se*. The pending claims are described in such a manner as to reasonably convey to one skilled in the art, at the time the application was filed, that the inventors were in possession of a process to screen a candidate substance for its ability to **bind** a recombinant mu opioid receptor polypeptide. Accordingly, for the above reasons, Applicants contend that the claims for the screening of a candidate substance for its ability to bind a mu opioid receptor are adequately described in the specification as filed and respectfully request that the rejection be withdrawn.

D. Claims 86-90, 92-99 and 101 are enabled by the specification

Claims 86-90, 92-99 and 101 are rejected under 35 U.S.C. §112, first paragraph, as the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. In particular, the Action states that Applicants provide no guidance or working examples of opioid receptors which are encoded for by as few as 35 contiguous bases of SEQ ID NO:7, nor is it predictable to one of ordinary skill in the art how to make a functional opioid receptor given that the receptor only needs to comprise anywhere from 11-33 contiguous amino acids of SEQ ID NO:8.

The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the specification coupled with information known in the art

without undue experimentation. Applicants note that the claimed process is for screening a substance for its ability to bind a recombinant mu opioid receptor polypeptide encoded by a nucleic acid sequence comprising at least 35 contiguous nucleotides of SEQ ID NO:7, including the guanine at nucleotide 389 of SEQ ID NO:7. For example, the process may identify an antibody that binds a recombinant opioid receptor polypeptide encoded for by a nucleic acid sequence of 35 contiguous nucleotides of SEQ ID NO:7, including the guanine nucleotide at position 389 of SEQ ID NO:7. The function of the recombinant mu opioid receptor polypeptide is irrelevant. Furthermore, the specification teaches the making and using of recombinant mu opioid receptor polypeptides, particularly chimeras, at least on page 38 lines 1-9 and pages 36–44. Also, numerous references cited within the specification describe methods of manipulating G-protein receptors known to those of skill in the art, such as adrenergic receptors. Thus, the preparation and use of a wide variety of recombinant opioid receptor polypeptides encoded by a nucleic acid sequence comprising at least 35 contiguous nucleotides of SEQ ID NO:7, including the guanine at nucleotide 389 of SEQ ID NO:7, was taught or known to one of skill in the art. The Examiner must presume the specification is enabling unless he can provide reasons to doubt the presumption. Here, no such reference or evidence is provided. The Examiner had not met his burden of providing **any** basis for rejecting the claims as not enabled, other than he does not agree with the Applicant's specification. This, however, is insufficient to maintain this rejection.

Accordingly, for the above reasons, Applicants contend that the claims are enabled for the screening of a candidate substance for its ability to bind a recombinant mu opioid receptor and respectfully request that the rejection be withdrawn.

E. Claims 86-90, 92-99 and 101 are definite.

1. Claim 85 is rejected as being indefinite.

Claim 85 is rejected as being confusing in that the term "intrinsic activation ability" is not understood. Applicants direct the Examiner to the specification, which states, "The interaction measured can be inter alia: the ability of the receptor to bind the candidate, the binding affinity , the intrinsic activation ability of the candidate[,] activation of ion channels in the cell membrane,...".(emphasis added). Webster's New Twentieth Century Dictionary of the English Language, second edition, defines "intrinsic" as "inherent", thus intrinsic activation ability is the inherent ability of the candidate substance to activate the receptor (see appendix C). Applicants have amended claim 85 to further clarify the claim.

2. Claims 86-90, 92-99 and 101 are rejected as being indefinite.

The Action rejects claims 86-90, 92-99 and 101 as being confusing as to whether the guanine at position 389 is within the nucleic acid sequence of SEQ ID NO:7. Applicants fail to understand the reasoning in the Action. The claim states in part: "...providing a recombinant opioid receptor polypeptide encoded by a nucleic acid sequence comprising at least 35 contiguous nucleotides of SEQ ID NO:7, including the guanine nucleotide at position 389 of SEQ ID NO:7...". The word "including" modifies the phrase "at least 35 contiguous nucleotides of SEQ ID NO:7", and thus the guanine at nucleotide position 389 is included within the "at least 35 contiguous nucleotides of SEQ ID NO:7", for example.

Accordingly, for the above reasons, Applicants contend that the claims are definite and respectfully request withdrawal of the rejection.

F. Claims 83-85 are not anticipated by Chen *et al.*

Claims 83-85 are rejected based the alleged lack of sufficiency of the Yu declaration. The Action inappropriately alleges that the three additional co-authors; Chen, Liu, and Hurley, were involved in the conception of the invention based on their alleged 'critical contribution' to reducing the invention to practice. Conception, not reduction to practice, is the proper standard for inventorship. Thus, the Action sets forth an improper standard for determining inventorship, *i.e.*, reduction to practice.

As set forth in the MPEP 2137.01 an inventor must contribute to the **conception** of the invention.

> "Unless a person contributes to the conception of the invention he/she is not an inventor...Insofar as defining an inventor is concerned, **reduction to practice, *per se*, is irrelevant**... [*Fiers v. Revel*, 984 F.2d 1164, 1168, 25 USPQ2d 1601, 1604-05 (Fed. Cir. 1993)]" (emphasis added).

The act of screening a library, sequencing DNA, and performing assays are routinely carried out on a daily basis in various laboratories by technicians and in some cases machines. Thus, screening a library, sequencing DNA, performing assay, *etc.* are by no means proof of **conception**, especially in light of the declaration submitted by the inventor. Furthermore, there is no requirement that the inventor be the one to reduce the invention to practice so long the reduction to practice is done on his behalf. The Action sets forth zero evidence contesting the validity of Dr. Yu's declaration. If such evidence is available to the Examiner Applicants request that such evidence be made of record.

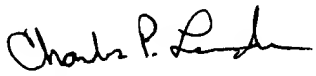
For the above reasons, Applicants contend that the Yu declaration establishes Dr. Yu as the sole inventor and the claims are not anticipated by Chen *et al.* Applicants respectfully request withdrawal of the rejection.

CONCLUSION

Applicant believes that the foregoing remarks fully respond to all outstanding matters for this application. Applicant respectfully requests that the rejections of all claims be withdrawn so they may pass to issuance.

Should the Examiner desire to sustain any of the rejections discussed in relation to this Response, the courtesy of a telephonic conference between the Examiner, the Examiner's supervisor, and the undersigned agent at 512-536-5674 is respectfully requested.

Respectfully submitted,



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